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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,206	06/21/2001	Sunao Hisada	400683	8134

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,206	HISADA ET AL.	
	Examiner	Art Unit	
	James L Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 9-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

Applicant's election with traverse of Group V, claim 8, in the paper filed 05 February 2004 is acknowledged. The traversal is on the ground(s) that the evidence does not support a serious burden on the Examiner to examine all claims together. This is not found persuasive because the explanations of the technical relationships and features of the inventions as grouped in the restriction requirement of record are sufficient to provide a *prima facie* showing of a serious burden upon the examiner. However, search of the method of detection, claims 1-5, with the elected method of providing the antibody therefor was not found burdensome by the examiner and the detection method was rejoined with the elected method for examination on the merits in the instant Office action. The requirement is still deemed proper for restriction of the alternative methods of antibody provision for the reasons of record. Newly submitted claims 11-21 are directed to an invention that is independent or distinct from the invention originally claimed and elected, lacking unity of invention therewith, for the following reasons: the original claims are independent and distinct from the invention of the newly submitted claims because the original claims do not share the technical feature of having at least one mutation of the CL or CH1 region in the antibody fragment as is now claimed as the original claims required antibody fragments of uniform isoelectric points, a feature not required in the newly submitted claims, and merely required adding a charged residue and/or

mutating only a residue in the CH1 region. Accordingly, claims 6, 7, and 9-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The disclosure is objected to because of the following informalities: the specification is replete with grammatical, idiomatic, and spelling errors too numerous to list specifically and should be carefully revised. Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 and 8 are method claims and, as such, they should conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim. These claims are confusing because the preamble recites quantitatively detecting an antigen but the body of the claims do not recite a step relating detecting fluorescence to quantitatively detecting an antigen.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-5 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Karger et al. (U.S. Pat. No. 5,348,633) in view of Fuchs et al. (U.S. Pat. No. 5,630,924) and Chen et al. (Electrophoresis 15: 13, 1994).

Karger et al. teach a method for quantitative detection of trace amounts of analyte wherein an antibody Fab' fragment specific for analyte is fluorescently labelled at a single reactive sulfhydryl group in a chemically-modified CH1/hinge region of the fragment, the fragment is reacted with sample to form an immune complex with any analyte present, the complex is concentrated and separated from unreacted components using capillary electrophoretic methods such as isoelectric focusing, and the concentrated and separated complex is quantitatively detected as an indication of level of analyte by detecting the level of the fluorescent signal of the immune complex. This is

shown by applicant in Figure 8 of the instant application as is set forth in the Japanese patent application of Karger et al. related to Pat. No. 5,348,633. In contrast to the invention as instantly claimed, the patent of Karger et al. does not disclose charge-modified antibodies having uniform isoelectric points.

Fuchs et al. teach that it was well known in the art that the electrophoretic mobility of a labelled antibody in capillary electrophoretic methods could be tailored by attaching charged groups to the labelled antibody (see e.g. col. 2), teach methods of labelling and charge modification of monoclonal antibody fragments, for example by the addition of charged amino acid sequences (see e.g. cols. 11-12), and teach that fragments could be purified before use by a method such as isoelectric focusing (see e.g. cols. 23-26).

Chen et al. teach that it is possible to achieve effective separation of antigen or antibody from antigen-antibody complexes by modulating the electrophoretic mobility of the antigen or antibody with modification with charge-bearing organic molecules (see e.g. page 14). The reference teaches that use of excess modified labelled monoclonal antibody in the capillary electrophoresis methods of the reference would require only a single antibody and obviate the need for a second sandwiching antibody (see e.g. page 21). Chen et al. is also cited in Fuchs et al.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have provided a charge-modified labelled monoclonal antibody fragment of uniform isoelectric point in the methods of Karger et al. because Fuchs et al. teach that charge modification of labelled antibody fragments was well known in the capillary electrophoresis art for a variety of

electrophoretic mobility tailoring purposes, such as to achieve effective separations with the use of a single charge-modified labelled monoclonal antibody as taught in Chen et al., and that purification of such antibody fragments can involve isoelectric focusing which one of ordinary skill in the art would have reasonably expected to have provided a uniform isoelectric point to the purified antibody fragment purified thereby. The process of providing a given reagent does not serve to differentiate an identical reagent provided by another method and there is nothing on the record which provides evidence of a difference between the antibody fragments of the prior art provided by chemical modifications and those as instantly claimed provided recombinantly.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 2 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karger et al. in view of Fuchs et al. and Chen et al. as applied to claims 1-5 and 8 above, and further in view of Bodmer et al. (WO 89/01974) and Cabilly et al. (U.S. Pat. No. 4,816,567).

The teachings of Karger et al., Fuchs et al., and Chen et al. are as set forth above and differ from the invention as instantly claimed in not teaching providing modified antibody fragments by recombinant methods.

Bodmer et al teach recombinant methods for making antibody molecules altered in the hinge region associated with the CH1 region of the molecule, in particular for reducing the number of cysteine residues to one for reporter molecule attachment (see e.g. page 7). The methods may also

substitute alternative sequences for those naturally present in a given antibody molecule hinge region. The reference teaches that methods of grafting complementarity determining regions onto other framework regions to produce chimeric antibodies were known to the art.

Cabilly et al. teach recombinant methods for the production of chimeric antibodies or antibody fragments for the benefits taught therein

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have produced the modified antibody fragments of Karger et al. in view of Fuchs et al. and Chen et al. recombinantly because Bodmer et al. teach the recombinant formation of antibody molecules with altered hinge regions having, in particular, a single reactive cysteine residue as desired for labelling by Karger et al. and Cabilly et al. teach the benefits of recombinant production of altered antibody molecules and fragments. One would have had obvious motivation to have produced cloned molecules for the benefits of providing a potentially unlimited source of homogeneous reagent for use and to obviate the need for periodic chemical modification of new batches of reagent for use.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

James L. Grun, Ph.D.
May 14, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641